UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/045,595	10/23/2001	Lino Tavares	208.1005US	8560

23280 7590 03/03/2005

DAVIDSON, DAVIDSON & KAPPEL, LLC
485 SEVENTH AVENUE, 14TH FLOOR
NEW YORK, NY 10018

EXAMINER	
GHALI, ISIS A D	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 03/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/045,595	TAVARES ET AL.	
	Examiner	Art Unit	
	Isis Ghali	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5,7-10,16-20,22-26,28,30-38 and 40-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-5,7-10,16-20,22-26,28,30-38 and 40-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/08/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The receipt is acknowledged of applicants' request for RCE, IDS, and request for extension of time, all filed 11/08/2004; and amendment, filed 12/02/2004.

Claims 2, 6, 11, 21, 27, 29 and 39 have been canceled.

Claims 1, 3-5, 7-10, 12-16, 20, 22-26, 28, 30-38 and 40-45 are included in the prosecution.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/08/2004 has been entered.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1, 3-5, 7-10, 12-16, 20, 22-26, 28, 30-38 and 40-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 93/10781 ('781) in view of US 5,091,186 (186).

WO '871 teaches method for treating hypertension and angina using felodipine (abstract). The reference disclosed that any suitable route of administration may be employed as for example transdermal patches (page 19, lines 28-34). The reference disclosed a pharmaceutical composition comprising felodipine in an acceptable carrier and other therapeutic ingredients (page 20, lines 1-6).

The reference does not teach the specific delivery profile claimed by the applicants. The reference does not teach the structure of the transdermal delivery system as claimed.

US '186 teaches a transdermal drug delivery device to deliver drugs at therapeutically effective rates for about 20-28 hours (abstract; col.6, lines 4-20; col.7, lines 29-40). The reference teaches the calcium channel blockers as one of the drugs to be delivered by the transdermal delivery device (col.5, line 10). The transdermal device comprises a flexible backing layer, an adhesive drug reservoir layer, and a release liner (col.3, lines 25-30, 6-63; col.4, line 43). The delivery profile of the drug is determined by the diffusivity of the drug in the reservoir layer, the solubility of the drug in the reservoir layer, and the degree of drug loading (col.6, lines 24-44). A given drug loading value will provide certain duration of delivery rate (col.7, lines 18-22). To achieve the known desirable blood level of the drug, the delivery rate of the drug ranges from 10-50 $ug/cm^2/hr$ (col.7, lines 47-51). The reservoir is pressure sensitive adhesive comprising rubbers, polysiloxane and polyurethanes (col.4, lines 33-40). The reservoir further comprises solvent and glycol, claimed by applicant as softening agent (col.6, line 1; col.7, line 55).

The claimed amounts of different ingredients in the reservoir layer do not impart patentability to the claims because it is within the skill in the art to select optimal parameters in order to achieve a beneficial effect. Thus, the claimed amounts of the drug, solvent and the softening agent are not considered critical, absent evidence to the contrary.

The selection of particular solvent and softening agent for a specific drug is within the skill of the art depending on the properties of the each drug and its intended use. Thus the solvents and softening agents claimed in claims 37, 38, 44, and 45, do not impart patentability to the presented claims, absent evident to the contrary.

The determination of the relative release rate via an in-vitro permeation test utilizing a Valia-Chien cell is known in the art and it is not part of the claimed method of treating hypertension and angina; or even a part of the transdermal device that provide particular plasma levels. It is only an in-vitro diagnostic test that is expected to provide the same results obtained from two similar delivery devices tested under the same circumstances, and the recitation of this in-vitro test does not impart patentability to claims directed to method of treating hypertension and angina or claims directed to transdermal device applied to patients to provide plasma levels, i.e. in vivo use.

Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention to treat hypertension and angina using a transdermal device comprising felodipine, as disclosed by WO '781, and provide the felodipine in the transdermal device disclosed by US '186 that provide a particular delivery profile of the drug, and manipulate the amount of the drug to obtain the desired delivery profile, motivated by the teaching of US '186 that a given drug loading value will provide a certain duration of delivery rate depending on the drug loading, with reasonable expectation of having a transdermal drug delivery device to deliver felodipine to treat hypertension and angina effectively.

Response to Arguments

Applicant's arguments filed 11/08/2004 have been fully considered but they are not persuasive. Applicants traverse the above obviousness rejection by arguing that WO '781 in view of Miranda, alone or in combination, do not teach all the aspects of the present claims including maintaining the transdermal device in contact with the skin for at least 3 days, providing the claimed mean relative release rate and plasma level of felodipine.

In response to the above argument, the examiner position is that WO '781 teaches method for treating hypertension and angina using felodipine, and Miranda teaches a delivery profile that can be determined by the diffusivity of the drug in the reservoir layer, the solubility of the drug in the reservoir layer, the degree of drug loading that will provide certain duration of delivery rate. The reference further teaches the achievement of the known desirable blood level of the drug, the delivery rate of the drug ranges from 10-50 ug/cm^2/hr, as claimed by applicants. It is expected to obtain the same plasma level from the transdermal patch that deliver felodipine to the skin at the same rate. Determination of the drug delivery profile and period of administration as well as the dose are within the skill of the art and it is controlled by many variables such as patient's age, weight, severity of the treated condition, etc. It is expected to obtain the same delivery profile from the device disclosed by the prior art if it has the same structure and the same amounts of different ingredients such as solvents and permeation enhancers. In considering the disclosure of the reference, it is proper to take into account not only the specific teachings of the reference but also the inferences

which one skilled in the art would reasonably be expected to draw therefrom. *In re Preda*, 401 F.2d 825, 826, 159 USPQ 342, 344 (CCPA 1968). The rational to modify or to combine the prior art does not have to be expressly stated in the prior art; the rational may be expressly or impliedly contained in the prior art or it may be reasoned from knowledge generally available to one of ordinary skill in the art.

5. Claims 37, 38, 44, and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO '781 in view of US '186 as applied to claims 1-16, 20-38 and 40-45 above, and further in view of US 5,240,711 ('711).

The teachings of WO '781 and US '186 are discussed above.

The combination of WO '781 and US '186 does not teach the specific solvents and specific softening agents as claimed in claims 37, 38, 44, and 45.

US '711 teaches a transdermal drug delivery device for controlled delivery of drug comprising backing layer, polymeric reservoir and protective liner. The reservoir comprising: 20-90% of polymeric material, 0.1-20% of the drug, 0.1-30% softener, and 0.1-30% of solvent (abstract; col.1, line 64-67; col.4, line 23). The reservoir is pressure sensitive adhesive and contains rubber-like co-, homo-, or block-copolymers (col.3, lines 25-26). The solvents used include those contain at least one acidic group, monoesters of dicarboxylic acids, such as monoethyl glutarate (col.4, lines 13-16). The softeners include medium chain triglycerides of the caprylic/capric acids or coconut oil; and dodecanol (col.3, lines 63-68; col.4, lines 1-2; col.7, lines 25-29). The backing is flexible, inflexible or aluminum foil (col.7, lines 5-12).

Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention to treat hypertension and angina using a transdermal device comprising felodipine that provides a specific delivery profile and having particular structure, and select the specific solvents and softening agents disclosed by US '711, motivated by the teaching of US '711 that the transdermal device having these particular ingredients in its reservoir layer provides a controlled delivery of the drug, with reasonable expectation of having a transdermal drug delivery device to deliver felodipine to treat hypertension and angina effectively.

Response to Arguments

Applicant's arguments filed 11/08/2004 have been fully considered but they are not persuasive. Applicants traverse the above rejection by arguing that US '711 fails to cure the deficiencies of the combination of WO '781 and Miranda.

In response to the above argument, the examiner position is US '711 is relied upon for the solely teaching of the solvents and softening agents that are known in the art and widely used in conventional transdermal devises for controlled release of drugs. In considering the disclosure of the reference, it is proper to take into account not only the specific teachings of the reference but also the inferences which one skilled in the art would reasonably be expected to draw therefrom. *In re Preda*, 401 F.2d 825, 826, 159 USPQ 342, 344 (CCPA 1968). The rational to modify or to combine the prior art does not have to be expressly stated in the prior art; the rational may be expressly or

impliedly contained in the prior art or it may be reasoned from knowledge generally available to one of ordinary skill in the art.

6. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. US 5,045,319 disclosed transdermal delivery system to deliver cardiovascular pharmaceuticals wherein the in-vitro release studies can be conducted using Valia-Chien diffusion cell. US 6,541,479 teaches the transdermal administration of calcium channel blockers including felodipine to treat hypertension and angina. US 2003/0199492 teaches the transdermal delivery of felodipine.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Isis Ghali whose telephone number is (571) 272-0595. The examiner can normally be reached on Monday-Thursday, 7:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic

Business Center (EBC) at 866-217-9197 (toll-free).

Isis Ghali
Examiner
Art Unit 1615

ISIS GHALI
PATENT EXAMINER